

in a minimum of 10 gal finish spray per acre. According to the Section 18 request, there is a maximum of 2 applications per season (0.2 - 0.25 lb ai/A/yr). However, the Nova[®] 40 W Section 18 supplemental label (page 2 of 2) says "Do not apply more than 1.25 lb of Nova 40W (0.5 lb ai myclobutanil) per acre per crop. There are approximately 60,000 acres with crop groups 6 & 7 in Florida which could require 15,000 lb ai for 2 applications at the maximum rate). The label directs occupational handlers to wear long sleeved shirt, long pants, shoes plus socks, protective eyewear and chemical resistant gloves. There is a 7 - 10 day retreatment interval and a 24 hr restricted entry interval. There is no preharvest interval. See Table 1.0 for a summary of the proposed use pattern.

Table 1.0 Summary of Proposed Section 18 Use of Myclobutanil

Crop Site	beans and peas
Pest	rust (<i>Phakopsora pachyrhizi</i>)
Formulation	Nova [®] 40 W (Reg. No. 62719-411), Rally [®] 40 W (Reg. No. 62719-411) 40 % ai myclobutanil in water soluble packages.
Application Method	groundboom, aerial, chemigation
Application Rate	0.1 - 0.125 lb a.i./A
Application Number	2 per crop season
Application Maximum	0.25 lb ai/A/season
Application Interval	7 - 10 days
Pre-Harvest Interval	0 days - may be applied until the day of harvest
Maximum acres treated	60,000 possible
Maximum a.i. used	If 60,000 acres are treated twice at 0.125 lb a.i./A, 1,500 total pounds of a.i. will be required.
Manufacturer	Dow CropSciences

OCCUPATIONAL PESTICIDE HANDLER EXPOSURE

The most highly exposed occupational pesticide handlers (i.e., mixers, loaders, applicators) are expected to be 1) mixer/loader loading water soluble packages in support of aerial operations, 2), applicator using open cab, ground boom sprayer, and aerial applicators. A "chemigator" is not assessed herein. For chemigation, there is no applicator in the strict sense. An individual prepares minibulk solution that is siphoned into the irrigation stream. Since the activity is similar to that of a mixer/loader, the assessment of a mixer/loader supporting aerial operations is used as a "worse case". Based upon the proposed use pattern and the expected number of acres

needing treatment, HED believes occupational handlers will be exposed to short-term duration (1 - 30 days) exposures. Ground applications are most likely conducted by private, i.e., grower handlers. Aerial application is expected to be done by "commercial" applicators.

Private (i.e., grower) applicators may perform all functions, that is, mix, load and apply the material. The HED Science Advisory Council for Exposure (ExpoSAC) directs that although the same individual may perform all those tasks, they shall be assessed separately. "By separating the two job functions, (i.e., mixing/loading from application) HED determines the most appropriate levels of personal protection equipment (PPE) for each aspect of the job without requiring an applicator to wear unnecessary PPE that may be required for mixer/loaders (e.g., chemical resistant gloves may only be necessary during the pouring of a liquid formulation)."

Chemical specific data were not available with which to assess pesticide handler exposure. Therefore surrogate data from studies in the Pesticide Handler Exposure Database Version 1.1 (August 1998) PHED SURROGATE EXPOSURE GUIDE were used to estimate mixer/loader and applicator exposure.

It is HED policy to assess handler exposure and risk using "baseline" PPE which is comprised of long-sleeved shirt, long pants, and shoes plus socks and if necessary to assess "baseline" **plus the use of protective gloves** or other PPE as might be necessary or appropriate.

On 12 August 1999 the HED Hazard Identification Assessment Review Committee (HIARC) met to discuss the adequacy of the toxicological database relative to myclobutanil (Memo, M. Copley, HED DOC NO 013740, "**MYCLOBUTANIL** - Second Report of the Hazard Identification Assessment Review Committee", 2 September 1999). RAB1 toxicologists re-evaluated the myclobutanil toxicology database and concluded that the 28-day dermal toxicity study previously used for short-term dermal risk assessment was not appropriate. A two-generation reproduction study in rats was selected. With regards to the assessment herein, the short-term duration (1 - 30 days) and the intermediate-term duration (1 - 6 months) dermal and inhalation toxicological endpoints are identified from a 2- generation reproduction toxicity study in the rat. The NOAEL is 10.0 mg ai/kg bw/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation. The HIARC identified a 50 % dermal absorption factor for use in assessing dermal exposures. Inhalation absorption is assumed to be 100 %. See Table 2.0 for a summary of exposures and risks to occupational pesticide handlers. See the ATTACHMENT for a summary of the toxicological endpoints used for risk assessment.

Table 2.0 Estimated Handler Exposure and Risk from the Use of Myclobutanil on Beans and Peas					
Unit Exposure ¹ mg a.i./lb handled	Applic. Rate ²	Units Treated ³ Per Day	Average Daily Dose ⁴ mg a.i./kg bw/day	NOAEL ⁵ mg a.i./kg bw/day	COMBINED MOE ⁶
<i>Mixer/Loader - Liquid Open-pour</i>					
Dermal: No Glove 2.9 LC With Glove 0.023 MC Inhal. 0.0012 HC	0.125 lb a.i./A	350 A	Dermal: No Glove 0.905 W Glove 0.007 Inhal 0.00075	Dermal 10 Inhalation 10	Dermal: No Glove 11 W Glove 1,300
<i>Applicator - Ground-boom - Open Cab</i>					
Dermal: No Glove 0.014 HC With Glove 0.014 MC Inhal 0.00074 HC	0.125 lb a.i./A	200 A	Dermal: No Glove 0.0025 W Glove 0.0025 Inhal 0.00026	Dermal 10 Inhalation 10	Dermal: No Glove 3,600 W Glove 3,600
<i>Aerial Applicator*</i> * Pilots not required to wear gloves					
Dermal: No Glove 0.0050 MC Inhal 0.000068 HC	0.125 lb a.i./A	350	Dermal: No Glove 0.00155 Inhal 0.000043	Dermal 10 Inhalation 10	Dermal: No Glove 6,300

1. Unit Exposures are taken from "PHED SURROGATE EXPOSURE GUIDE", Estimates of Worker Exposure from The Pesticide Handler Exposure Database Version 1.1, August 1998. Dermal = Single Layer Work Clothing No Gloves; Single Layer Work Clothing With Gloves; Inhal. = Inhalation. Units = mg a.i./pound of active ingredient handled. Data Confidence: LC = Low Confidence, MC = Medium Confidence, HC = High Confidence.

2. Applic. Rate. = Taken from the Florida Section 18 request.

3. Units Treated are taken from "Standard Values for Daily Acres Treated in Agriculture"; SOP No. 9.1. Science Advisory Council for Exposure; Revised 5 July 2000.

4. Average Daily Dose = Unit Exposure * Applic. Rate * Units Treated * 0.5 (% dermal absorption) ÷ Body Weight (70 kg).

5. NOAEL = No Observable Adverse Effect Level: short- and intermediate term dermal and inhalation NOAEL = 10 mg a.i./kg bw/day.

6. COMBINED Margin of Exposure = No Observable Adverse Effect Level (NOAEL) ÷ ADD. Since the dermal and inhalation NOAELs are the same, are identified from the same study, and cite the same toxicological effects, the dermal and inhalation exposures are summed (combined) and then divided into the NOAEL.

A MOE of 100 is adequate to protect occupational pesticide handlers. Provided mixer/loaders use protective gloves, all MOEs are > 100. Therefore the proposed use does not exceed HED's level of concern.

POST-APPLICATION EXPOSURE TO AGRICULTURAL WORKERS

There is a potential for agricultural workers to experience post-applications exposures to pesticides during the course of typical agricultural activities. HED in conjunction with the Agricultural Re-entry Task Force (ARTF) has identified a number of post-application agricultural activities that may occur. HED has also identified Transfer Coefficients (TC) expressed as cm^2/hr which help describe the amount of foliar dislodgeable pesticide residue that is available to be transferred to agricultural workers during the course of post-application agricultural activities.

There were no chemical specific data with which to estimate post-application exposures of agricultural workers to dislodgeable residues of propiconazole. Therefore, theoretical estimates of exposure, based on surrogate studies, have been conducted. The ExpoSAC (SOP 003.1, Rev. 7 Aug. 2000. Regarding Agricultural Transfer Coefficients; Amended ExpoSAC Meeting notes - 13 Sept 01) lists a number of possible post-application agricultural activities relative to field corn that result in pesticide exposure to agricultural workers. Transfer Coefficients (TC) expressed as cm^2/hr are identified for each of the post-application, agricultural activities. The TCs are derived from data in surrogate exposure studies conducted during the various activities listed.

The highest TC identified for dried peas and beans 2,500 cm^2/hr which is for hand harvesting. For this assessment, HED uses the 2,500 cm^2/hr TC for a Tier I, screening level estimate.

The transfer coefficients used in this assessment are from an interim transfer coefficient procedure developed by HED's ExpoSAC using proprietary data from the Agricultural Re-Entry Task Force (ARTF) database (Standard Operating Procedure # 3.1). It is the intention of HED's ExpoSAC that this procedure will be periodically updated to incorporate additional information about agricultural practices in crops and new data on transfer coefficients. Much of this information will originate from exposure studies currently being conducted by the ARTF, from further analysis of studies already submitted to the Agency, and from studies in the published scientific literature.

Post-application worker exposure is estimated using HED procedure that assumes 20% of the application rate is available as dislodgeable foliar residue on the day of treatment. HED expects post-application agricultural exposures to scouts (i.e., crop advisors) or workers involved in irrigation would typically be short-term. The total number of acres treated per day is comparatively small and treatment is not expected to be necessary at the same time for all acres on a given farm, therefore scouting after treatment will occur in short-term periods of time.

$\text{PDR}_t = \text{DFR}_t * \text{CFI} * \text{Tc} * \text{ET}$ where:

PDR_t = potential dose rate on day "t" (mg/day)

DFR_t = dislodgeable foliar residue on day "t" ($\mu\text{g}/\text{cm}^2$)

CFI = weight unit conversion factor to convert μg units in DFR value to mg for the daily dose (0.001 $\text{mg}/\mu\text{g}$)

TC = transfer coefficient (cm^2/hr) (In this case 2,500 cm^2/hr ; ExpoSAC SOP 003.1 Rev. 7

Aug. 2000; amended 13 Sept 01 ExpoSAC meeting Notes).
ET = Exposure Time (hrs) (8)

and

$DFR_t = AR * F * (1-D)^t * CF2 * CF3$ where:

AR = Application rate (lb a.i./A) (0.125 lb a.i./A)

F = fraction of a.i. retained on foliage (unitless)

D = fraction of residue that dissipates daily (unitless)

t = postapplication day on which exposure is being assessed

CF2 = weight unit conversion factor to convert the lbs a.i. in the application rate to μg for the DFR value ($4.54 \times 10^8 \mu\text{g/lb}$)

CF3 = Area unit conversion factor to convert the surface area units (ft^2) in the application rate to cm^2 for the DFR value ($1.08 \times 10^{-3} \text{ ft}^2/\text{cm}^2$ or $2.47 \times 10^{-8} \text{ acre}/\text{cm}^2$ if the application rate is per acre).

$$\therefore DFR = 0.125 \text{ lb a.i./A} * 0.20 * (1-0)^0 * 4.54 \times 10^8 \mu\text{g a.i./lb} * 2.47 \times 10^{-8} \text{ A}/\text{cm}^2 = 0.28 \mu\text{g}/\text{cm}^2$$

$$\begin{aligned} PDR &= 0.28 \mu\text{g}/\text{cm}^2 * 0.001 \text{ mg}/\mu\text{g} * 2,500 \text{ cm}^2/\text{hr} * 8 \text{ hr}/\text{day} = 5.6 \text{ mg a.i.}/\text{day} \div 70 \text{ kg bw} = \\ &0.08 \text{ mg a.i.}/\text{kg bw}/\text{day} * 0.5 (\% \text{ dermal absorption}) = 0.04 \text{ mg ai}/\text{kg bw}/\text{day} \end{aligned}$$

Margin of Exposure (MOE) = NOAEL \div PDR

$$\therefore 10 \text{ mg a.i.}/\text{kg bw}/\text{day} \div 0.04 \text{ mg a.i.}/\text{kg bw}/\text{day} = 250.$$

An MOE of 100 is adequate to protect agricultural workers from post-application exposure to myclobutanil. The calculated MOE > 100 therefore this use does not exceed HED's level of concern.

RESTRICTED ENTRY INTERVAL (REI)

Myclobutanil is classified in Acute Toxicity Category IV for acute dermal, acute inhalation and primary skin irritation. It is classified in Category I for primary eye irritation and it is a "Positive" dermal sensitizer. The Rally[®] label lists the REI as 24 hours.

Title 40 of the Code of Federal Regulations, § 156.208 (c) (2) states: If a product contains only one active ingredient and it is in toxicity category I by the criteria in paragraph (c) (1) of this section, the restricted-entry interval shall be 48 hours." The Federal Register Vol. 57, No. 163, 21 August 1992 page 38104 and 38142 (For 40 CFR Parts 156 and 170) indicates that "...a 48-hour REI is established for any product containing an active ingredient that is in toxicity category I (most acutely toxic category) because of dermal toxicity or skin or eye irritation." HED suggests that the RD confirm or correct, as may be necessary, the 24 hour REI listed on the product label

ATTACHMENT

Acute Toxicity of Myclobutanil

Guideline No.	Study Type	MRID #(S)	Results	Toxicity Category
81-1	Acute Oral	00141662	LD ₅₀ = 1.6 g/kg (M) LD ₅₀ = 2.29 g/kg (F)	III
81-2	Acute Dermal	00141663	LD ₅₀ > 5000 mg/kg	IV
81-3	Acute Inhalation	40357101	LC ₅₀ > 5.1 m/L	IV
81-4	Primary Eye Irritation	00141663	Severe eye irritant	I
81-5	Primary Skin Irritation	00141663	Non-irritating to skin	IV
81-6	Dermal Sensitization	40357102	Positive sensitizer	

The doses and toxicological endpoints selected for various exposure scenarios are summarized below.

EXPOSURE SCENARIO	DOSE (mg/kg/day)	ENDPOINT	STUDY
Acute Dietary <u>females 13-50 years of age</u>	NOAEL = 60 UF = 100	LOAEL = 200 mg/kg/day based on increased resorptions, decreased litter size and a decrease in the viability index.	Developmental Toxicity - rabbit
	Acute RfD = 0.60		
Acute Dietary <u>general population</u> including infants and children	none		
	Acute RfD = none		
Chronic Dietary	NOAEL = 2.49 mg/kg/day UF = 100	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat
	Chronic RfD = 0.025 mg/kg/day		
Short-Term (Dermal)	oral NOAEL = 10 mg/kg/day ¹	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Intermediate-Term (Dermal)	oral NOAEL = 10 mg/kg/day ¹	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during	2 Generation Reproduction Toxicity - rat

		lactation.	
Long-Term (Dermal)	oral NOAEL =2.49 mg/kg/day ¹	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat
Short Term (Inhalation)	oral NOAEL=10 mg/kg/day ²	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Intermediate Term (Inhalation)	oral NOAEL=10 mg/kg/day ²	LOAEL = 50 mg/kg/day based on atrophy of the testes and prostate as well as an increase in the number of stillborn pups and a decrease in pup weight gain during lactation.	2 Generation Reproduction Toxicity - rat
Long Term (Inhalation)	oral NOAEL =2.49 mg/kg/day ²	LOAEL = 10 mg/kg/day based on decreased testicular weights and increased testicular atrophy.	Chronic Toxicity/ Carcinogenicity - rat

¹ Use the appropriate dermal absorption factor (50%) since the NOAEL is from an oral study.

² Use the appropriate absorption factor (100%) since the NOAEL is from an oral study.

NOTE: ATTACHMENT taken from: Memo, M. Copley, "MYCLOBUTANIL: - Second Report of the Hazard Identification Assessment Review Committee", HED DOC NO 013740, 2 SEPT 1999 and amended per RAB1 toxicologists.

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